UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

April 9, 1999
MEMORANDUM

SUBJECT: **Phostebupirim**. Dietary Risk Assessment Update.
PC Code: 129086
DP Barcode: D254704

FROM: Christina Jarvis, Environmental Protection Specialist
Reregistration Branch II
Health Effects Division (7509C)

THRU: Pauline Wagner, Branch Chief
Reregistration Branch II
Health Effects Division (7509C)

TO: Amy Caicedo
Special Review Branch
Special Review and Reregistration Division (7508W)

Background:

Bayer Corporation submitted acute and subchronic neurotoxicity studies in the rat for the organophosphorus chemical phostebupirim; however, these studies were not reviewed prior to the *Comprehensive Review of the Organophosphates* meeting on May 12-14, 1998. Because these studies were not available at the time of the meeting, the requirements for the acute and subchronic neurotoxicity studies in the rat were viewed as data gaps. Consequently, an FQPA safety factor of 3X was retained for phostebupirim.

These neurotoxicity studies have since been reviewed and are found to be acceptable. Since Bayer Corporation has satisfied the requirements for the acute and subchronic neurotoxicity studies in the rat, the FQPA Safety Factor Committee has removed the 3X safety factor. This memorandum updates the HED dietary risk assessment for phostebupirim, with particular consideration for the requirements of the 1996 Food Quality Protection Act (FQPA).

Attachments include the Hazard Identification Assessment Review Committee (HIARC) report (R. Fricke memo, 04/07/99), the dietary exposure analysis (C. Christensen memo,

04/06/99), the FQPA Safety Factor Committee report (B. Tarplee memo, 03/30/99, hard copy only), and the Drinking Water Assessment (P. Jennings memo, 12/8/97, hard copy only).

Hazard Identification:

Phostebupirim (O-[2-(1,1-dimethylethyl)-5-pyrimidinyl] O-ethyl O-(1-methylethyl) phosphorothioate) is an organophosphorus insecticide registered by Bayer Corporation (formerly Miles, Inc.) for the control of corn rootworms, cutworms, and other soil insect pests in corn commodities (forage and fodder, pop, and sweet). Formulations include the 93% liquid Technical (3125-411), Aztec 2.1% Granular Insecticide (3125-412), and Aztec 4.67% Granular Insecticide (3125-513). Aztec 4.67% Granular Insecticide was registered on October 22, 1998 and is for use only with a SmartBox® applicator system.

The toxicology database for phostebupirim is adequate according to the Subdivision F Guideline requirements for a food-use chemical. In summary, technical phostebupirim is acutely toxic (category 1) for oral, dermal, and inhalation toxicity. Toxicity categories of 2 (acute oral), 3 (acute dermal, acute inhalation, and primary eye irritation), and 4 (primary dermal irritation) are assigned to Aztec 4.67% granular. Aztec 4.67% granular is not a dermal sensitizer.

The toxicity endpoints selected for risk assessment are based primarily on plasma, red blood cell, and brain cholinesterase inhibition. Phostebupirim is classified as a Group E chemical, indicating that it is "Not Likely" to be carcinogenic in humans via relevant routes of exposure. This classification is supported by adequate carcinogenicity studies in rats and mice.

Dermal absorption is assumed to be 100%. On December 3, 1998, the HIARC met to re-evaluate the dermal absorption factors used for 16 organophosphates. For phostebupirim, the Committee determined that a dermal absorption value of 100% is appropriate since comparison of the 21-day dermal toxicity study and the oral developmental toxicity study (both in rabbits) indicates high toxicity by both routes at very low dose levels (1 mg/kg/day or less).

Considerations for special sensitivity in infants and children (FQPA):

On September 30, 1997, the HIARC met to evaluate the toxicology data base of phostebupirim with special consideration for the developmental, reproductive, and neurotoxicity data. These data were re-evaluated in order to address the sensitivity of infants and children to phostebupirim, as required by the FQPA. Developmental toxicity studies in rats and rabbits showed no evidence of additional sensitivity in young rats or rabbits following pre- or postnatal exposure to phostebupirim, and comparable NOAELs were established for adults and offspring. The results of the two-generation reproduction study in rats showed no increased sensitivity in pups over adults. However, the potential for increased susceptibility to phostebupirim in infants and children could not be adequately defined because of data gaps which existed for acute and subchronic neurotoxicity studies in the rat. The requirement for a developmental neurotoxicity study was placed in reserve status pending submission and review of the neurotoxicity studies.

On March 25, 1999, the HIARC re-visited phostebupirim in order to evaluate the acute and subchronic neurotoxicity studies in the rat. These studies were found to be acceptable and meet guideline requirements. Data gaps for acute and subchronic neurotoxicity studies in the rat have been adequately fulfilled. In addition, no treatment-related neuropathology was seen in

studies conducted in hens and rats. Based on the weight-of-evidence, the HIARC determined that a developmental neurotoxicity study in rats *is not* required.

The FQPA Safety Factor Committee met on March 29, 1999 to re-evaluate the hazard and exposure data for phostebupirim, and recommended that the FQPA Safety Factor (as required by the Food Quality Protection Act of August 6, 1996) be removed in assessing the risk posed by this chemical. The Committee concluded that the safety factor could be removed for the following reasons:

(1) The toxicology database is adequate for phostebupirim.

(2) There is no indication of increased susceptibility of rats or rabbits to phostebupirim. In the developmental and reproduction toxicity studies, effects in the fetuses/offspring were observed only at or above treatment levels which resulted in evidence of parental toxicity.

(3) The HIARC determined that a developmental neurotoxicity study in rats is not required.

(4) Adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary exposure and to provide a screening level drinking water exposure assessment (there are no registered residential uses for phostebupirim).

Endpoints selected for risk assessment:

Acute: The endpoint selected from the acute neurotoxicity study in rats for acute dietary risk assessment is based on plasma and red blood cell cholinesterase inhibition at 1.5 hours post-dosing. The LOAEL is 0.5 mg/kg/day (NOAEL not achieved in males).

The acute neurotoxicity study used for acute dietary risk assessment purposes is a more realistic exposure scenario than the developmental study in the rabbit, which was used for acute dietary risk assessment purposes in the original risk assessment (S. Robbins memo, 2/16/95). The acute neurotoxicity study shows effects after a single dose, whereas the developmental study shows effects (plasma and red blood cell cholinesterase inhibition) only after nine doses.

The revised acute RfD is 0.002 mg/kg/day. An uncertainty factor of 300 is required due to inter- and intraspecies variation (100X) and lack of a NOAEL (3X). Since the HED FQPA Safety Factor Committee removed the FQPA safety factor, the acute RfD is identical to the Population Adjusted Dose[1] (0.002 mg/kg/day).

Chronic: The endpoint selected for chronic dietary risk assessment is based on plasma, red blood cell, and brain cholinesterase inhibition in dogs at 0.13 mg/kg/day. The NOAEL is 0.02 mg/kg/day.

The revised chronic RfD is 0.0002 mg/kg/day. An uncertainty factor of 100 is required due to inter- and intraspecies variation. Since the HED FQPA Safety Factor Committee removed the

[1]Population Adjusted Dose (PAD) = RfD (acute or chronic)/FQPA Safety Factor

FQPA safety factor, the chronic RfD is identical to the PAD (0.0002 mg/kg/day).

Product Chemistry Data Requirements:

In the product chemistry review of 9/19/94 (M. Nelson), CBTS (Chemistry Branch Tolerance Support) indicated the modifications made by the petitioner (Bayer Corporation, formerly Miles Inc.) to the manufacturing process of Phostebupirim Technical (3125-411) triggered the need for additional product chemistry data. On 10/5/94, Bayer submitted data to explain why and what modifications were made to its manufacturing process. Upon review of this data, CBTS concluded that no significant changes to the manufacturing process of Phostebupirim Technical appear to be involved (memo dated 12/8/94, from M. Nelson to M. Mautz/R. Forrest).

Dietary Exposure Residue Estimates for Risk Assessment:

The nature of the residue in corn plants has been adequately delineated. The residue of concern for regulatory purposes is the parent phostebupirim only.

The nature of the residue in ruminants has been adequately delineated. The residue of concern (based on observed residues) for regulatory purposes is phostebupirim (MAT 7484), and its oxygen analog OMAT. However, regulation of residues in animal commodities is not needed at this time.

The nature of the residue in poultry has been adequately delineated. The residue of concern for regulatory purposes (based on observed residues) is the parent phostebupirim only. However, for the sake of consistency with the observed residue of concern in ruminants, both phostebupirim and OMAT should be regulated in poultry. Regulation of residues in animal commodities is not needed at this time.

No detectable residues (<0.01 ppm) of phostebupirim or OMAT were shown to occur in any corn commodity from the crop field trials or the processing study. Accordingly, conventional feeding studies (ruminant, poultry) were not conducted. In this instance, the metabolism studies submitted (goat, hen) also serve as feeding studies. The metabolism studies demonstrate that there is no likelihood of secondary residues occurring in meat, milk, poultry, or eggs as a result of the proposed use on corn (category 3 of 40 CFR 180.6(a) applies). There is no need for tolerances or analytical methods for meat, milk, poultry, or eggs in conjunction with the proposed use on corn.

Dietary Risk Estimates:

DEEM (Dietary Exposure Evaluation Model), based on food consumption data from the USDA Continuing Survey of Food Intake by Individuals (CFSII) from 1989-92, was used to estimate acute and chronic dietary exposure to phostebupirim. DEEM, which replaces DRES, is used to estimate exposure to constituents in foods comprising the diets of the U.S. population, including population subgroups, and assumes uniform distribution of phostebupirim in the food supply. A summary of the residue information considered in this acute and chronic dietary analysis is included in attachment 2.

Acute risk: The acute analysis for phostebupirim is a Tier 1, or upper-end, estimate of dietary exposure, with all residues at tolerance levels and 100 percent of the commodities assumed to be

treated with phostebupirim. The percent of the acute RfD utilized for the highest exposed subpopulation (children 1-6 years old) at the 95th percentile is 4.79%.

Based on calculated risk estimates, the acute dietary risks associated with the use of phostebupirim on corn appear to be minimal and do not exceed the acute RfD for any of the DEEM population subgroups. The results of the acute analysis are shown in attachment 2.

Chronic risk: The chronic analysis for phostebupirim is a Tier 1, or upper-end, estimate of dietary exposure, with all residues at tolerance levels and 100 percent of the commodities assumed to be treated with phostebupirim. The percent of the chronic RfD utilized for the highest exposed subpopulation (children 1-6 years old) is 17.6%.

Based on calculated risk estimates, the chronic dietary risks associated with the use of phostebupirim on corn appear to be minimal and do not exceed the chronic RfD for any of the DEEM population subgroups. The results of the chronic analysis are shown in attachment 2.

The DEEM analysis indicates that consumers of corn commodities with residues of phostebupirim at the tolerance level of 0.01 ppm will have an acute and chronic exposure that is significantly below the RfD for all population subgroups.

Drinking water exposure considerations:

The environmental fate database for phostebupirim is incomplete (unresolved issues with field dissipation studies); based on the available data, the parent compound appears to be quite persistent and immobile in soil. The OMAT metabolite, however, appears to be quite mobile.

No monitoring data for phostebupirim are available. Therefore, environmental fate data were used in the following screening level models to calculate the drinking water estimated concentrations (DWECs) for phostebupirim: GENEEC (Tier 1) model for surface water and SCI-GROW (Tier 1) for ground water.

OPP has calculated drinking water levels of comparison (DWLOCs) for acute exposure to phostebupirim in surface and ground water for the U.S. general population and children (ages 1-6). These DWLOCs are 68.355 ppb and 19.04 ppb, respectively. For chronic (non-cancer) exposure to phostebupirim in surface and ground water, the DWLOCs are 6.475 ppb for the U.S. general population, and 1.65 ppb for children (ages 1-6).

Estimated maximum concentrations of phostebupirim in surface and ground water are 1.89 ppb and 0.3 ppb, respectively. Estimated average concentrations of phostebupirim in surface and ground water are 0.86 ppb and 0.3 ppb, respectively. [Note: the average concentration of phostebupirim in surface water can be divided by a factor of 3 prior to comparison with the chronic DWLOC; therefore, the average concentration for surface water is 0.86 ppb/3, or 0.287 ppb]. The maximum and average DWECs in surface and ground water are less than OPP's levels of comparison for phostebupirim in drinking water.

OPP concludes with reasonable certainty that residues of phostebupirim in drinking water are less than calculated drinking water levels of comparison and, therefore, do not result in an unacceptable level of risk.

Conclusions:

Potential acute or chronic dietary exposure (including drinking water) to adults and children from phostebupirim is negligible and does not pose a risk of concern.

Attachments:

Attachment 1: HIARC report, R. Fricke memo, 04/07/99
Attachment 2: Dietary Exposure Analysis, C. Christensen memo, 04/06/99
Attachment 3: FQPA report, B. Tarplee memo, 03/30/99 (hard copy only)
Attachment 4: Drinking Water Assessment, P. Jennings memo, 12/8/97 (hard copy only)

DATE: **March 17, 1999**

MEMORANDUM

SUBJECT: **Phostebupirim (129086): Reassessment of Acute and Chronic RfDs**

FROM: Robert F. Fricke
Reregistration Branch II
Health Effects Division (7509C)

THROUGH: Alan Nielsen, Branch Senior Scientist
Reregistration Branch II
Health Effects Division (7509C)

TO: Pauline Wagner
Reregistration Branch II
Health Effects Division (7509C)

and

Jesudoss Rowland
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

1. Background: Bayer Corporation submitted acute (MRID: 43473001) and subchronic (MRID: 43656302) neurotoxicity studies in the rat, but were not reviewed prior to the Comprehensive Review of the Organophosphates meeting on May 12, 13, and 14, 1998. Because these studies were not available at the time of the meeting, the requirements for the acute and subchronic neurotoxicity studies in the rat were viewed as data gaps. As a result of the data gaps, an FQPA Safety Factor of a 3X was retained. The current endpoints and doses used for acute and chronic risk assessments are summarized in Table 1.

Table 1: Current Endpoints and Doses for Use in Acute and Chronic Risk Assessment

	Acute	Chronic

Critical Study	Developmental Rabbit Study (MRID 42005455 and 42981901)	1-Year Dog Feeding Study (MRID 42005452 and 42119301)
Endpoint	Plasma and RBC ChEI [a] at gestation day 14	Plasma, RBC and brain ChEI
NOAEL	0.1 mg/kg/day	0.02 mg/kg/day
UF	UF=100 10X inter- and 10X intraspecies variation	UF=100 10X inter- and 10X intraspecies variation
RfD	0.001 mg/kg/day	0.0002 mg/kg/day
FQPA Safety Factor	Reduced to 3X	Reduced to 3X
PAD [b]	**0.0003 mg/kg/day**	**0.00007 mg/kg/day**

a ChEI = Cholinesterase Inhibition

b PAD = Population Adjusted Dose $= \frac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

2. Results of Neurotoxicity Studies: The acute and subchronic neurotoxicity studies in the rat were reviewed and found to be acceptable. The guideline requirements, §81-8 and §82-5(b), have been satisfied. The results of these studies are briefly summarized in Table 2.

Table 2: Results of Acute and Subchronic Neurotoxicity Studies in the Rat

	Acute Neurotoxicity Study	**Subchronic Neurotoxicity Study**
Doses Tested	Male: 0, 0.5, 1.0, 5.0 mg/kg Female: 0, 0.25, 0.5, 1.0 mg/kg	Male: 0, 0.26,1.2 and 4.4 mg/kg/day Female: 0, 0.30, 0.96, and 3.6 mg/kg/day
NOAEL	Males: Not established Females: 0.25 mg/kg	Not established
LOAEL	Males: 0.5 mg/kg Females: 0.5 mg/kg	Males: 0.26 mg/kg/day Females: 0.30 mg/kg/day
Basis for LOAEL	% ChEI Plasma / RBC / Brain Males 26* / 20* / 3 (ns) Females 31* / 32* / 9 (ns) At 1.5 hr post-dosing	% ChEI Day / Plasma / RBC / Brain Male 24 / 5 (ns) / 66* / --- Female 25 / 26* / 69* / --- Male 87 / 40* / 66* / 7* Female 88 / 27* / 72* / 13*

a ChEI = Cholinesterase Inhibition, * $p \leq 0.05$ vs control, ns = not significant, --- Not measured

3. Recommendation to the HIARC: Since Bayer Corporation has satisfied the requirements for acute and subchronic neurotoxicity studies in the rat, the 3X FQPA safety factor should be

removed. It is further recommended that the acute neurotoxicity study in the rat be used to establish the acute dietary risk assessment. The acute (single dose) study is a more realistic exposure scenario than the developmental study in the rabbit, which showed effects (plasma and RBC ChEI) only after nine doses. Based on these findings, the following endpoints and doses for acute and chronic risk assessment are recommended to the committee:

Table 3: Proposed Doses and Endpoints for Acute and Chronic Dietary Risk Assessment

	Acute	**Chronic**
Critical Study	Acute Neurotoxicity Study in the Rat (MRID 43473001)	1-Year Dog Feeding Study (MRID 42005452 and 42119301)
Endpoint	Plasma and RBC ChEI [a] at 1.5 hr post-dosing	Plasma, RBC and brain ChEI
NOAEL	0.5 mg/kg (LOAEL) NOAEL not achieved in males	0.02 mg/kg/day
Uncertainty Factor	UF= 300 100X inter- and intraspecies variation and 3X lack of NOAEL	UF=100 100X inter- and intraspecies variation
RfD	**0.002 mg/kg**	**0.0002 mg/kg/day**
FQPA Safety Factor	**1 (FQPA factor removed)**	**1 (FQPA factor removed)**
PAD [b]	**0.002 mg/kg** (Same as acute RfD)	**0.0002 mg/kg/day** (Same as chronic RfD)

a ChEI = Cholinesterase Inhibition

b PAD = Population Adjusted Dose $= \frac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

cc Christina Jarvis (HED/RRB II, 7509C)
Brenda Tarplee (HED/SAB, 7509C)
Jacqueline McQueen (SRRD, 7508W)

MEMORANDUM

Subject:

Acute and Chronic Dietary Exposure and Risk Analysis for Phostebupirim (PC code 129086); DP Barcode D254707

From:

Carol Christensen, EPS
Reregistration Branch II
Health Effects Division (7509C)

Through:

Pauline Wagner, Chief
Reregistration Branch II
Health Effects Division (7509C)

To:

Christina Jarvis, Risk Assessor
Reregistration Branch II
Health Effects Division (7509C)

Action Requested

An acute and chronic dietary exposure and risk assessment was requested to determine the risks associated with the reregistration uses of Phostebupirim on corn. In this assessment, there are no changes to published tolerances.

Executive Summary

In this analysis, a Tier I acute and chronic dietary exposure and risk assessment was performed to determine the risk associated with the uses of phostebupirim on sweet corn and field corn which are supported through the re-registration process. The assessment utilized tolerance level residues to estimate the dietary exposure of phostebupirim in the diets of the U.S. population as well as certain sub-populations and assumed that 100% of the crop(s) were treated with the chemical. The risks associated with these uses do not exceed the Agency's level of concern. The acute dietary risk is 5% of the RfD (PAD) for the most highly exposed sub-population, children 1-6. The chronic dietary risk is 17% of the RfD (PAD) for the most highly exposed sub-population, children 1-6.

Toxicological Endpoints

The Hazard Identification Assessment and Review Committee (HIARC) discussed the hazard endpoint selection for phostebupirim acute and chronic dietary exposure and risk assessment (R. Fricke, 3/17/99). Prior to this meeting, Bayer Corporation submitted acute and subchronic neurotoxicity studies in the rat which were reviewed and found to be acceptable. The registrant satisfied all requirements for acute and subchronic neurotoxicity studies in the rat. Therefore, the HIARC recommended to the FQPA Safety Factor Committee that the FQPA factor not be retained (FQPA factor = 1). In a meeting on March 29, 1999 the FQPA committee accepted the HIARC recommendation and removed the safety factor. The following are the toxicological endpoints used for the acute and chronic dietary risk assessment.

	Acute	Chronic
Critical Study	Acute Neurotoxicity Study in the Rat	1-year Dog Feeding Study
Endpoint	Plasma and RBC ChEI[a] at 1.5 hr post-dosing	Plasma, RBC and brain ChEI[a]
NOAEL	0.5 mg/kg (LOAEL) NOAEL not achieved in males	0.02 mg/kg/day
Uncertainty Factor	UF=300 100x inter- and intraspecies variation and 3x lack of NOAEL	UF=100 100X inter- and intraspecies variation
RfD	0.002 mg/kg	0.0002 mg/kg/day
FQPA Safety Factor	1 (FQPA Safety Factor removed)	1 (FQPA Safety Factor removed)
PAD[b]	0.002 mg/kg (Same as acute RfD)	0.0002 mg/kg/day (Same as chronic RfD)

a ChEI - cholinesterase inhibition
b PAD = population adjusted dose RfD/FQPA Safety Factor

Residue Information

The published tolerances for phostebupirim are located at 40 CFR 180.483. Tolerances are listed for:

Corn, forage and fodder0.01 ppm
Corn, pop0.01 ppm
Corn, sweet0.01 ppm

There are no additions or revocations of crops or crop groups included in the re-registration document nor are there any recommended changes to the tolerance. The last risk assessment performed for phostebupirim (HED Risk Assessment, 2/16/95) stated that metabolism studies demonstrate that there is no reasonable likelihood of secondary residues occurring in meat, milk, poultry, or eggs as a result of the use of phostebupirim of corn (category 3 of 40 CFR 180.6(a)

applies). Therefore, this dietary assessment includes only tolerance level residues on the above corn products.

The acute and chronic dietary exposure assessment used published tolerance level residue values and assumed 100% of the crop is treated. In this case, the acute and the chronic residue values are identical.

Results and Discussion

The acute and chronic dietary exposure and risk assessments were performed using the Dietary Exposure Evaluation Model (DEEM ™). DEEM can be used to estimate exposure to constituents in foods comprising the diets of the US population, including population subgroups. The software contains food consumption data from the USDA Continuing Survey of Food Intake by Individuals (CFSII) from 1989-1992. A summary of the residue information considered in this acute and chronic analysis is attachment 1.

Acute Exposure Analysis (Tier I)
The detailed acute dietary risk analysis estimates the distribution of single day exposures for the overall U.S. population and certain subgroups. The analysis evaluates exposure to the chemical for each food commodity and assumes uniform distribution of phostebupirim in the food supply.

The aRfD is derived from the lowest exposure at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group along with the application of uncertainty factors. The percent of the aRfD is calculated as the ratio of the exposure value to the RfD (exposure/aRfD x 100 = % aRfD). The population adjusted dose (PAD) is the ratio of the aRfD and the FQPA safety factor for sensitivity of infants and children, for all populations which include infants and children. For phostebupirim, since the HED FQPA Safety Factor Committee determined to remove the 10x Safety Factor, the RfD is identical to the PAD. For the acute dietary exposure analysis of phostebupirim, exposure (consumption) was compared to an acute population adjusted dose of 0.002 mg/kg-bw/day (B. Tarplee, 3/30/99) which reflects an FQPA factor of 1. The acute dietary risks associated with the use of phostebupirim on corn do not exceed the Agency's level of concern. The results of this analysis is shown in attachment 2.

Chronic Exposure Analysis (Tier I)

A chronic exposure analysis was performed utilizing the DEEM ™ exposure modeling software. The input values include the reassessed tolerance level residues for commodities on which phostebupirim is used.

The RfD is derived from an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control along with the application of uncertainty factors. The percent of the RfD is calculated as the ratio of the exposure value to the RfD (exposure/RfD x

100 = % RfD). The population adjusted dose (PAD) is the ratio of the RfD and the FQPA safety factor for sensitivity of infants and children, for all populations which include infants and children. For phostebupirim, since the HED FQPA Safety Factor Committee determined to remove the 10x Safety Factor, the RfD is identical to the PAD. Exposure (consumption) was compared to the chronic population adjusted dose of 0.0002 mg/kg-bw/day (B. Tarplee, 3/30/99) which reflects an FQPA safety factor of 1. The chronic dietary risk associated with the use of phostebupirim on corn do not exceed the Agency's level of concern. The results of this analysis are shown in attachment 3.

Attachment 1 - Residue File Listing
Attachment 2 - Acute Dietary Exposure and Risk Assessment
Attachment 3 - Chronic Dietary Exposure and Risk Assessment

ATTACHMENT 1

U.S. Environmental Protection Agency Ver. 6.12
DEEM89N CHRONIC analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086R Adjustment factor #2 NOT used.
Analysis Date 03-25-1999 Residue file dated: 03-25-1999/15:21:21/8
Reference dose (RfD, CHRONIC) = 0.000200 mg/kg body-wt/day
COMMENT 1: published tol.; no changes in reassessment

Residue file listing

Food Code	EPA Code	Crop Group	Food Name	Residue (ppm)	Adj. Fctrs #1	#2
237	15004AA	O	CORN/POP	0.010000	1.00	1.00
238	15005AA	O	CORN/SWEET	0.010000	1.00	1.00
266	24002EA	O	CORN GRAIN-ENDOSPERM	0.010000	1.00	1.00
267	24002HA	O	CORN GRAIN-BRAN	0.010000	1.00	1.00
268	24002SA	O	CORN GRAIN/SUGAR/HFCS	0.010000	1.50	1.00
289	27002OA	O	CORN GRAIN-OIL	0.010000	1.00	1.00
388	24002MO	O	CORN GRAIN/SUGAR-MOLASSES	0.010000	1.50	1.00

ATTACHMENT 2

U.S. Environmental Protection Agency Ver. 6.27
DEEM ACUTE analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086r.R91 Adjustment factor #2 NOT used.
Analysis Date: 03-25-1999/15:33:52 Residue file dated: 03-25-1999/15:21:21/8
Acute Reference Dose (aRfD) = 0.002000 mg/kg body-wt/day
Run Comment: published tol.; no changes in reassessment
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Summary calculations:

	95th Percentile Exposure	95th Percentile % aRfD	99th Percentile Exposure	99th Percentile % aRfD	99.9 Percentile Exposure	99.9 Percentile % aRfD
U.S. pop - all seasons:	0.000047	2.33	0.000085	4.25	0.000149	7.45
U.S. pop - spring season:	0.000044	2.19	0.000083	4.14	0.000139	6.95
U.S. pop - summer season:	0.000049	2.45	0.000092	4.60	0.000158	7.89
U.S. pop - autumn season:	0.000046	2.29	0.000085	4.23	0.000149	7.44
U.S. pop - winter season:	0.000048	2.38	0.000082	4.10	0.000143	7.15
Northeast region:	0.000043	2.14	0.000082	4.09	0.000135	6.76
Midwest region:	0.000051	2.55	0.000091	4.53	0.000153	7.65
Southern region:	0.000047	2.37	0.000085	4.25	0.000152	7.62
Western region:	0.000045	2.23	0.000079	3.94	0.000148	7.41
Hispanics:	0.000045	2.27	0.000088	4.38	0.000138	6.89
Non-hispanic whites:	0.000046	2.28	0.000082	4.11	0.000148	7.42
Non-hispanic blacks:	0.000054	2.68	0.000093	4.65	0.000149	7.47
Non-hispanic other:	0.000044	2.21	0.000078	3.88	0.000138	6.92
All infants (<1 year):	0.000081	4.03	0.000122	6.08	0.000206	10.32
Nursing infants (<1 year):	0.000025	1.26	0.000037	1.87	0.000041	2.07
Non-nursing infants (<1 yr):	0.000089	4.46	0.000137	6.85	0.000213	10.63
Children (1-6 years):	0.000096	4.79	0.000142	7.09	0.000214	10.68
Children (7-12 years):	0.000068	3.39	0.000093	4.65	0.000139	6.97
Females (13+/preg/not nsg):	0.000027	1.35	0.000035	1.75	0.000051	2.55

ATTACHMENT 2 (cont.)

U.S. Environmental Protection Agency Ver. 6.27
DEEM ACUTE analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086r.R91 Adjustment factor #2 NOT used.
Analysis Date: 03-25-1999/15:33:52 Residue file dated: 03-25-1999/15:21:21/8
Acute Reference Dose (aRfD) = 0.002000 mg/kg body-wt/day

Summary calculations:

	95th Percentile Exposure	% aRfD	99th Percentile Exposure	% aRfD	99.9 Percentile Exposure	% aRfD
Females (13+/nursing):	0.000037	1.84	0.000045	2.25	0.000047	2.37
Females (13-19 yrs/np/nn):	0.000038	1.91	0.000064	3.19	0.000096	4.80
Females (20+ years/np/nn):	0.000027	1.37	0.000047	2.35	0.000087	4.34
Females (13-50 years):	0.000031	1.56	0.000050	2.48	0.000090	4.49
Males (13-19 years):	0.000048	2.40	0.000080	3.99	0.000110	5.51
Males (20+ years):	0.000030	1.51	0.000048	2.39	0.000077	3.87
Seniors (55+):	0.000025	1.23	0.000039	1.95	0.000085	4.26
Pacific Region:	0.000041	2.07	0.000071	3.56	0.000130	6.51

ATTACHMENT 3

U.S. Environmental Protection Agency Ver. 6.12
DEEM89N CHRONIC analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086R Adjustment factor #2 NOT used.
Analysis Date 03-25-1999 Residue file dated: 03-25-1999/15:21:21/8
Reference dose (RfD, CHRONIC) = 0.000200 mg/kg body-wt/day
COMMENT 1: published tol.; no changes in reassessment

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Pop - 48 states - all seasons	0.000015	7.4%
U.S. Population - spring season	0.000014	7.2%
U.S. Population - summer season	0.000016	7.8%
U.S. Population - autumn season	0.000015	7.5%
U.S. Population - winter season	0.000014	7.0%
Northeast region	0.000014	6.8%
Midwest region	0.000016	7.8%
Southern region	0.000016	7.8%
Western region	0.000014	6.8%
Pacific Region	0.000013	6.4%
Hispanics	0.000015	7.3%
Non-hispanic whites	0.000015	7.3%
Non-hispanic blacks	0.000017	8.4%
Non-hispanic other than black or white	0.000013	6.6%
All infants (<1 year)	0.000018	8.9%
Nursing infants (<1 year)	0.000006	2.9%
Non-nursing infants (<1 year)	0.000023	11.5%
Children (1-6 years)	0.000035	17.6%
Children (7-12 years)	0.000027	13.3%
Females (13-19 yrs/not preg. or nursing)	0.000015	7.3%
Females (20+ years/not preg. or nursing)	0.000010	4.8%
Females (13-50 years)	0.000011	5.5%
Females (13+/pregnant/not nursing)	0.000011	5.3%
Females (13+/nursing)	0.000012	6.0%
Males (13-19 years)	0.000019	9.3%
Males (20+ years)	0.000011	5.4%
Seniors (55+)	0.000009	4.3%